Wnt7b is an important intrinsic regulator of hair follicle stem cell homeostasis and hair follicle cycling.

Journal: Stem Cells

Publication Year: 2013

Authors: Eve Kandyba, Krzysztof Kobielak

PubMed link: 24222445

Funding Grants: CIRM Stem Cell Biology Training Program

Public Summary:
In this study we examine the role of Wnt7b during hair follicle (HF) development and hair follicle stem cell (hfSCs) activation during the transition from the resting, telogen phase to the actively growing, anagen phase of the hair cycle. For the first time, we reveal that Wnt7b is an important signaling component required for maintaining proper HF growth during the hair cycle as mice lacking Wnt7b protein in the skin produce hair around ~30% shorter than controls. Our findings also demonstrate that Wnt7b is a key factor required for hfSCs activation, HFs lacking Wnt7b demonstrated a significant delay in activation (which could not be compensated for by other Wnt proteins) remaining in a resting state longer than control HF. In addition, we reveal that Wnt7b-deficient hfSCs retain stem cell characteristics and can regenerate new hfSCs populations during the HF cycle but do so with slower self-renewal, perturbing growth entry in the next HF cycle. This data supports our previous model (Kandyba et al., PNAS 2013) that Bone Morphogenetic Protein (BMP) inhibition regulates ligand-dependent Wnt activation in hfSCs and demonstrates Wnt7b as a novel protein which mediates this link directly. Overall, this work highlights the intrinsic dynamic competition between Wnt/BMP signaling and provides the platform for extrinsic influence providing multiple hierarchical layers to control stem cells. Together, these findings emphasize the key importance of Wnt7b in maintaining proper HF cycle length and regulating hfSCs activation to fuel HF regeneration. This work received prestigious “Faculty of 1000” recognition.

Scientific Abstract:
The hair follicle (HF) is an exceptional mini-organ to study the mechanisms which regulate HF morphogenesis, cycling, hair follicle stem cell (hfSCs) homeostasis and progeny differentiation. During morphogenesis, Wnt signaling is well characterized in the initiation of HF patterning but less is known about which particular Wnt ligands are required and whether individual Wnt ligands act in an indispensable or redundant manner during postnatal hfSCs anagen onset and HF cycle progression. Previously, we described the function of the Bone morphogenetic protein (BMP) signaling target gene WNT7a in intrinsic regulation of hfSCs homeostasis in vivo. Here, we investigated the role of Wnt7b, which was also intrinsically up-regulated in hfSCs during physiological and precocious anagen after BMP inhibition in vivo. We demonstrated Wnt7b to be a direct target of canonical BMP signaling in hfSCs and using Wnt7b conditional gene targeting during HF morphogenesis revealed disrupted HF cycling including a shorter anagen, premature catagen onset with overall shorter hair production and diminished HF differentiation marker expression. Additionally, we observed that postnatal ablation of Wnt7b resulted in delayed HF activation, affecting both the HG and bulge hfSCs but still maintaining a two-step sequence of HF stimulation. Interestingly, Wnt7b cKO hfSCs participated in re-formation of the new HF bulge, but with slower self-renewal. These findings demonstrate the importance of intrinsic Wnt7b expression in hfSCs regulation and normal HF cycling and surprisingly reveal a non-redundant role for Wnt7b in the control of HF anagen length and catagen entry which was not compensated by other Wnt ligands. Stem Cells 2013.